

Docket No.: 84495-US1
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Lee James Johnson et al.

Application No.: 10/673,352

Confirmation No.: 8469

Filed: September 30, 2003

Art Unit: 1744

For: MICROELECTRONIC CELL
ELECTROPORATION ARRAY

Examiner: N. A. Bowers

AMENDED APPEAL BRIEF

MS Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

In response to the paper mailed on August 27, 2008, the appeal brief has been amended to include 5 separate headings under “The Ground of Rejections to be Reviewed on Appeal”, as requested. The “Arguments” section has been amended to reflect the headings as well.

This brief contains items under the following headings as required by 37 C.F.R. § 41.37 and M.P.E.P. § 1206:

- | | |
|------------|---|
| I. | Real Party In Interest |
| II | Related Appeals and Interferences |
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I. REAL PARTY IN INTEREST

The real party in interest for this appeal is:

The Government of the United States of America, as represented by The Secretary of the Navy

II. RELATED APPEALS, INTERFERENCES, AND JUDICIAL PROCEEDINGS

There are no other appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in this appeal.

III. STATUS OF CLAIMS

A. Total Number of Claims in Application

There are 7 claims pending in application

B. Current Status of Claims Claims canceled: 1-20

1. Claims withdrawn from consideration but not canceled: None
2. Claims pending: 21-27
3. Claims allowed: None
4. Claims rejected: 21-27

C. Claims On Appeal:

The claims on appeal are claims 21-27

III. STATUS OF AMENDMENTS

Applicant did not file an Amendment After Final Rejection.

IV. SUMMARY OF CLAIMED SUBJECT MATTER

The present invention is drawn to device employing electroporation, or more specifically spatially targeted entry of substances into objects with surrounding membranes employing electroporation.

An aspect of the present invention is to provide a microelectronic stimulator array 101 as illustrated in Figure 1. Figure 2 depicts a cathode 212 and an anode 213, when an electric field is applied across the cathode 212 and the anode 213, this causes ions 210 to move and attract extracellular ions through a cell membrane 214. (please note discussion on page 6 paragraph 0025 and 0027)

Independent claim 21 recites a device (for example as illustrated in Figure 3) for use with a voltage source, a fluid having a substance (please see item 321 of Figure 3, and discussion on page 7, lines 30-32), and a plurality of objects (please see items 320, and discussion on page 7, lines 28-30), each of the objects having a surrounding membrane that prevents the substance from passing therethrough without electroporation, said device comprising: a fluid chamber (please note discussion on page 7 paragraph 0028) operable to receive the fluid; a stimulator array (please note discussion on page 8 paragraph 0031) comprising at least one anode (please see item 501 of Figure 5 and see discussion on page 8 paragraph 0031) and at least one cathode (please see item 501 of Figure 5 and see discussion on page 8 paragraph 0031), said stimulator array structured for connection to the voltage source; and a conducting portion having a first side (please note discussion on page 7 paragraph 0028 and Figure 3) and a second side (please note discussion on page 7 paragraph 0028 and Figure 3), said first side being in electrical contact with one of said at least one anode and said at least one cathode, said second side being disposed to receive a layer of the plurality of objects, wherein when said at least one anode comprises only a single anode (please note Figure 5D item 504 and see discussion on page 8 paragraph 0031), said at least one cathode

comprises more than one cathode, wherein when said at least one cathode comprises only a single cathode (please see Figure 5D item 503 and see discussion on page 8 paragraph 0031), said at least one anode comprises more than one anode, wherein said conducting portion is disposed such that said second side is disposed between said first side and the fluid when the fluid is received in said fluid chamber, and wherein, when the second side has the layer of the plurality of objects thereon (please note discussion on page 7 paragraph 0028 and please see Figure 3 frames B and C), when the fluid is in said fluid chamber and when the voltage source provides voltage to said stimulator array, said stimulator array is operable to generate spatially variant voltages to said conducting portion to enable the substance to pass through membranes of a spatially variant portion of the plurality of objects via electroporation (please note discussion on page 7 paragraph 0028 and see Figure 3, frames B and C).

GROUND OF REJECTION TO BE REVIEWED ON APPEAL

The first ground of rejection to be reviewed on appeal, with reference to the Office Action dated March 22, 2007, paragraph 1, is whether claims 24 and 27 comply with 35 U.S.C. § 112, first paragraph?

The second ground of rejection to be reviewed on appeal, with reference to the final Office Action dated March 22, 2007, paragraph 2, is whether claim 21 complies with 35 U.S.C. § 112, second paragraph?

The third ground of rejection to be reviewed on appeal, with reference to the final Office Action dated March 22, 2007, paragraph 3, is whether claim 21 (and therefore are dependent claims 22-27) is anticipated by United States Patent Application 20050054969 to Hoff with respect to 35 U.S.C. § 102(e)?

The fourth ground of rejection to be reviewed on appeal, with reference to the final Office Action dated March 22, 2007, paragraph 4, is whether claim 21 (and therefore dependent claims 23-27) is obvious (35 U.S.C. § 103(a)) with respect to United States Patent Application 20050054969 in view of United States Patent Application 20060206161 to Nicolelis and/or Dzekunov (United States Patent Application 20040197883).

The fifth ground of rejection to be reviewed on appeal, with reference to the final Office Action dated March 22, 2007, paragraph 5, is whether claim 22 is obvious (35 U.S.C. § 103(a)) with respect to United States Patent Application 20050054969 in view of United States Patent Application 20060206161 to Nicolelis and/or Dzekunov (United States Patent Application 20040197883) and in further view of Merritt (United States Patent Application 20040241965).

V. ARGUMENT

The first ground of rejection to be reviewed on appeal, with reference to the Office Action dated March 22, 2007, paragraph 1, is whether claims 24 and 27 comply with 35 U.S.C. § 112, first paragraph?

With respect to the first ground of rejection to be reviewed, it is respectfully submitted that claims 24 and 27 comply with 35 U.S.C. § 112, first paragraph.

Paragraph 1 of the final Office action (Office action) dated March 22, 2007, asserts that the “specification does not describe an embodiment in which only a single cathode or a single anode used [sic].” The Office action then further asserts that the “entirety of the written description and drawing point only to examples in which a plurality of cathodes and a plurality of anodes are utilized.” Both of the above-discussed assertions are incorrect. Applicants respectfully point out that lines 6-14 of paragraph [0031] of the substitute specification filed January 18, 2007, clearly state many embodiments that include a single electrode of one type and a plurality of electrodes of another type. For example, as illustrated in FIG. 5B, “one unit cell is the cathode 503 and 8 others are used as the anode 504.” Further, as illustrated in FIG. 5D, “a unit cell is used as the cathode 507 and the top of the chamber is used as the anode 508.” Additionally, as further described in lines 12-

14 of paragraph [0031], a “unit cell or a group of unit cells would be activated to act as either the cathode or the anode and the large plate would be activated to be the opposing electrode.” Accordingly, in light of the above discussion the specification does describe an embodiment in which a single anode and a single cathode are employed.

The second ground of rejection to be reviewed on appeal, with reference to the final Office Action dated March 22, 2007, paragraph 2, is whether claim 21 complies with 35 U.S.C. § 112, second paragraph?

Turning to the second ground of rejection to be reviewed, it is respectfully submitted that claim 21 complies with 35 U.S.C. § 112, second paragraph.

Paragraph 2 of the Office action indicates that lines “10-13 state that the at least one anode comprises only a single anode, but then later state that the at least one anode comprises more than one anode.” The cited portion of the Office action further indicates that “it is uncertain whether a plurality of anodes/cathodes or a singular anode/cathode is claimed.”

It is respectfully submitted that claim 21 clearly recites in lines 10-11 that “**when** said at least one anode comprises only a single anode, said at least one cathode comprises more than one cathode.” (*emphasis added*) Further, claim 21 clearly recites in lines 12-13 that “**when** said at least one cathode comprises only a single cathode, said at least one anode comprises more than one anode.” (*emphasis added*) It is clear that the scope of the invention recited in claim 21 includes instances wherein there is a single anode and instances wherein there is a single cathode. In the instances that there is a single cathode, it is clear that the scope of the invention recited in claim 21 requires more than one anode. Similarly, in the instances that there is a single anode, it is clear that the scope of the invention recited in claim 21 requires more than one cathode. This subject matter is supported, for example, with reference to lines 6-14 of paragraph [0031] of the substitute specification filed January 18, 2007, wherein many embodiments include a single electrode of one type and a plurality of electrodes of another type. Furthermore, the embodiments are highlighted in Figure 5 A-D.

In light of the above discussion, it is respectfully submitted that claim 21 complies with 35 U.S.C. § 112, second paragraph.

The third ground of rejection to be reviewed on appeal, with reference to the final Office Action dated March 22, 2007, paragraph 3, is whether claim 21 (and therefore are dependent claims 22-27) is anticipated by United States Patent Application 20050054969 to Hoff with respect to 35 U.S.C. § 102(e)?

Turning to the third ground of rejection to be reviewed, It is respectfully submitted that independent claim 21 and dependent claims 22-27 are not anticipated over the cited prior art.

As illustrated in FIGs. 3A-3E, and as described in the specification as filed, for example on page 7, a plurality of substances can be loaded into specifically targeted and spatially varied cells. The present invention enables such a feature as a result of the chamber that accepts the fluid, and the conducting portion. Specifically, the chamber is disposed such that when the fluid is in the chamber, the fluid is in contact with the cells. Further, the conducting portion is disposed to receive a layer of the cells and is operable to pass spatially variant voltages to targeted cells for electroporation. Once the targeted cells have been electroporated, the chamber may be emptied and then refilled with a new fluid. This feature is recited in independent claim 21.

Independent claim 21 recites, *inter alia*, the conducting portion is disposed such that the second side is disposed between the first side and the fluid when the fluid is received in said fluid chamber, and wherein, when the second side has the layer of the plurality of objects thereon, **when the fluid is in said fluid chamber** and when the voltage source provides voltage to said stimulator array, **said stimulator array is operable to generate spatially variant voltages to said conducting portion to enable the substance to pass through membranes of a spatially variant portion of the plurality of objects via electroporation.**

It is clear from the language of the claim that the recited structure (including the recited spatial relationship between the recited elements) gives rise to recited function. Hoff fails to disclose the above-identified limitations, specifically, Hoff fails to disclose a conducting portion having a second side being disposed to receive a layer of a plurality of objects that are to have a

substance disposed therein through electroporation. Accordingly, Hoff additionally fails to disclose that when the second side of the conducting portion has a layer of the plurality of objects thereon, the stimulator array is operable to generate spatially variant voltages to the conducting portion to enable the substance to pass through the membranes of a spatially variant portion of the plurality of objects via electroporation.

Paragraph 3 of the Office action fails to address the above-identified limitations. Page 8 of the Office action states it “is not understood why Applicant does not consider the electrodes of Hoff to be legitimate ‘conducting portions’ because the electrodes are in direct contact with the cells.” Applicants have not argued whether the electrodes of Hoff are “legitimate” conducting portions. Nevertheless, the recited relationship between the recited fluid chamber, the stimulator array and the conducting portion of claim 21 is not disclosed in Hoff.

Hoff fails to disclose the explicitly recited structure that includes functional recitations of the elements, i.e., the conducting portion is disposed such that the second side is disposed between the first side and the fluid when the fluid is received in said fluid chamber, and wherein, when the second side has the layer of the plurality of objects thereon, **when the fluid is in said fluid chamber** and when the voltage source provides voltage to said stimulator array, **said stimulator array is operable to generate spatially variant voltages to said conducting portion to enable the substance to pass through membranes of a spatially variant portion of the plurality of objects via electroporation.**

Claim 21 requires the stimulator array to be able to pass the fluid through a membrane when the fluid is in the fluid chamber. First of all, the Office action fails to point out a disclosure of a stimulator array in Hoff. In the event that one of microplungers 18 of Hoff is considered a fluid chamber as recited in claim 21, when the fluid is in the microplunger 18, an unidentified stimulator array would be unable to enable the fluid to pass through membranes. Accordingly, Hoff fails to disclose that which is recited in claim 21.

In light of the above, it is clear that Hoff fails to anticipate independent claim 21 within the meaning of 35 U.S.C. § 102(e).

The fourth ground of rejection to be reviewed on appeal, with reference to the final Office Action dated March 22, 2007, paragraph 4, is whether claim 21 (and therefore dependent claims 23-27) is obvious (35 U.S.C. § 103(a)) with respect to United States Patent Application 20050054969 in view of United States Patent Application 20060206161 to Nicolelis and/or Dzekunov (United States Patent Application 20040197883).

Turning now to the rejection of claims 21-27 under 35 U.S.C. § 103(a). Neither Nicolelis, Dzekunov disclose the shortcomings of Hoff such that a combination of Hoff, Nicolelis, Dzekunov would render independent claim 21 obvious within the meaning of 35 U.S.C. § 103(a). Specifically, similar to Hoff, none of Nicolelis, Dzekunov discloses a conducting portion having a second side being disposed to receive a layer of a plurality of objects that are to have a substance disposed therein through electroporation. Accordingly, Nicolelis, Dzekunov additionally fail to disclose that when the second side of the conducting portion has a layer of the plurality of objects thereon, the stimulator array is operable to generate spatially variant voltages to the conducting portion to enable the substance to pass through membranes of a spatially variant portion of the plurality of objects via electroporation.

Accordingly, Nicolelis, Dzekunov, fail to disclose the shortcomings of Hoff such that a combination of Hoff, Nicolelis, Dzekunov would suggest that which is recited in independent claim 21. Therefore, claim 21 is patentable over a combination of Hoff, Nicolelis, Dzekunov within the meaning of 35 U.S.C. §103. Further, claims 22-27 are dependent upon claim 21 and therefore include all the limitations thereof. For at least this reason, claims 22-27 are additionally patentable over a combination of Hoff, Nicolelis, Dzekunov within the meaning of 35 U.S.C. §103.

In light of the above, it is respectfully submitted that independent claim 21 and dependent claims 22-27 are patentable over the cited prior art, and it is respectfully requested that the outstanding rejections under 35 U.S.C. §§ 102 and 103 be withdrawn.

The fifth ground of rejection to be reviewed on appeal, with reference to the final Office Action dated March 22, 2007, paragraph 5, is whether claim 22 is obvious (35 U.S.C. §

103(a)) with respect to United States Patent Application 20050054969 in view of United States Patent Application 20060206161 to Nicolelis and/or Dzekunov (United States Patent Application 20040197883) and in further view of Merritt (United States Patent Application 20040241965.

Turning now to the rejection of claim 22 under 35 U.S.C. § 103(a). Neither Nicolelis, Dzekunov and Merritt disclose the shortcomings of Hoff such that a combination of Hoff, Nicolelis, Dzekunov and Merritt would render independent claim 21 obvious within the meaning of 35 U.S.C. § 103(a). Specifically, similar to Hoff, none of Nicolelis, Dzekunov and Merritt discloses a conducting portion having a second side being disposed to receive a layer of a plurality of objects that are to have a substance disposed therein through electroporation. Accordingly, Nicolelis, Dzekunov and Merritt additionally fail to disclose that when the second side of the conducting portion has a layer of the plurality of objects thereon, the stimulator array is operable to generate spatially variant voltages to the conducting portion to enable the substance to pass through membranes of a spatially variant portion of the plurality of objects via electroporation.

The final Office action recites, on page 7, “it is known in the art to utilize indium bumps to make electrical connections...” It is of no consequence whether “indium bumps” can make electrical connections, because, it is respectfully submitted that, Merritt, Nicolelis, and Dzekunov, fail to disclose the shortcomings of Hoff such that a combination of Hoff, Nicolelis, Dzekunov and Merritt would fail to suggest that which is recited in dependent claim 22.

Therefore, claim 22 is patentable over a combination of Hoff, Nicolelis, Dzekunov within the meaning of 35 U.S.C. §103.

In light of the above, it is respectfully submitted that independent claim 21 and dependent claims 22-27 are patentable over the cited prior art, and it is respectfully requested that the outstanding rejections under 35 U.S.C. §§ 102 and 103 be withdrawn.

VI. CLAIMS

A copy of the claims involved in the present appeal is attached hereto as Appendix A. As indicated above, the claims in Appendix A do include the amendments filed by Applicant on January 18, 2007.

Dated: September 20, 2007

Respectfully submitted,

Electronic signature: /Aisha Ahmad/
Aisha Ahmad

Registration No.: 47,381
US NAVAL RESEARCH LABORATORY
4555 Overlook Ave, SW
Washington, DC 20375
(202) 404-1557
(202) 404-7380 (Fax)
Attorney For Applicant

APPENDIX A

Claims Involved in the Appeal of Application Serial No. 10/673,352

21. A device for use with a voltage source, a fluid having a substance, and a plurality of objects, each of the objects having a surrounding membrane that prevents the substance from passing therethrough without electroporation, said device comprising:

a fluid chamber operable to receive the fluid;

a stimulator array comprising at least one anode and at least one cathode, said stimulator array structured for connection to the voltage source; and

a conducting portion having a first side and a second side, said first side being in electrical contact with one of said at least one anode and said at least one cathode, said second side being disposed to receive a layer of the plurality of objects,

wherein when said at least one anode comprises only a single anode, said at least one cathode comprises more than one cathode,

wherein when said at least one cathode comprises only a single cathode, said at least one anode comprises more than one anode,

wherein said conducting portion is disposed such that said second side is disposed between said first side and the fluid when the fluid is received in said fluid chamber, and

wherein, when the second side has the layer of the plurality of objects thereon, when the fluid is in said fluid chamber and when the voltage source provides voltage to said stimulator array, said stimulator array is operable to generate spatially variant voltages to said conducting portion to enable the substance to pass through membranes of a spatially variant portion of the plurality of objects via electroporation.

22. The device according to claim 21, further comprising:

indium bumps,

wherein said conducting portion comprises microwire glass and is connected to said stimulator array via said indium bumps.

23. The device according to claim 21, further comprising:
a pump; and
tubing in communication with said pump and said fluid chamber,
wherein said fluid chamber comprises sidewalls, an inflow port, outflow ports, and valves to prevent back flow, and
wherein said pump is operable to pump the fluid into the fluid chamber via said tubing.
24. The device according to claim 21, wherein said at least one anode comprises a single anode.
25. The device according to claim 21, wherein said stimulator array comprises alternating rows of anodes and cathodes.
26. The device according to claim 21, wherein said stimulator array comprises a plurality anodes and a plurality of cathodes, and
wherein each cathode is surrounded by a number of anodes.
27. The device according to claim 21, wherein said at least one cathode comprises a single cathode.

APPENDIX B

Evidence entered by the Examiner and relied upon by the appellant in appeal.

United States Patent Application No. 2005/0054969 A1 to Hoff was entered into the record by the Examiner on page 3 of an Office Action mailed on Oct. 31, 2006. United States Patent Application No. 2006/0206161 A1 to Nicolelis was entered into the record by the Examiner on page 5 of an Office Action mailed on Oct. 31, 2006. United States Patent Application No. 2004/0197883 A1 to Dzekunov was entered into the record by the Examiner on page 5 of an Office Action mailed on Oct. 31, 2006. United States Patent Application No. 2004/0241965 A1 to Merritt was entered into the record by the Examiner on page 7 of an Office Action mailed on Oct. 31, 2006.

APPENDIX C

No related proceedings are referenced in II. above, hence copies of decisions in related proceedings are not provided.